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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR            | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/724,178      | 12/01/2003  | Stephen William Watson Michnick | ODDY 007            | 8945             |

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06/07/2005

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EXAMINER

BRUSCA, JOHN S

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/724,178

Applicant(s)

WATSON MICHNICK ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 March 2005.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,6,7,10,12,13 and 15-19 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1,6,7,10,12,13 and 15-19 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. It is brought to the applicant's attention that the Declaration of Stephen William Watson Michnick under 37 CFR 1.132 filed 14 March 2005 consistently refers to publication numbers as applications that correspond to the publication number. The declaration has been interpreted to refer to publication numbers that correspond to application numbers as discussed throughout the declaration.
2. It is noted that the Office action mailed 20 October 2004 stated that the elected species of SEQ ID NOS: 583 and 609 were related as polynucleotide and encoded polypeptide, however the sequences are different polypeptide fragments of fluorescent proteins.

#### ***Election/Restrictions***

3. Applicant's election without traverse of species SEQ ID NOS: 583 and 609 in the reply filed on 14 March 2005 is acknowledged.

#### ***Specification***

4. The objection to the specification in the Office action mailed 20 October 2004 is withdrawn in view of the amendment to the abstract filed 14 March 2005.
5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the following reasons:

Several nucleotide sequences appear in the specification in figure 2 that are not properly identified. Nucleotide sequences must be identified by sequence identification number. Furthermore, if said sequences do not appear in the sequence listing, a new listing including said

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sequences must be supplied. It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02). If said sequences consist of a portion of sequences already of record in the sequence listing, they may be identified in the specification using the existing SEQ ID No. accompanied by the position of the sequence on the already listed sequence.

Applicants are required to comply with all the requirements of 37 CFR §§ 1.821-1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

***Claim Rejections - 35 USC § 112***

6. The rejection of claims 4 and 11 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in the Office action mailed 20 October 2004 is withdrawn in view of the amendment canceling the claims filed 14 March 2005.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

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determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must use fluorescent protein fragments SEQ ID NOS: 583 and 609 in a protein fragment complementation assay (PCA). For the reasons discussed below, there would be an unpredictable amount of experimentation required to use the claimed polypeptides in a PCA assay.

b) The specification provides guidance to form fragments of the same fluorescent reporter protein in a PCA assay on pages 13, 14, and 20-34. The specification does not provide any specific guidance to use the combination of SEQ ID NOS: 583 and 609 in a PCA assay. On page 42 the specification describes the table of SEQ ID NOS in the appendix as mutant fragments of fluorescent proteins. The specification only describes SEQ ID NO: 583 as "Venus F1DX F46L E64L M153T mutations" and SEQ ID NO:609 as "Venus F2DX V163A S175G mutations." The specification appears to show that the two polypeptides are fragments of different proteins.

c) The specification provides working examples of using fragments of the same fluorescent protein in a PCA assay on pages 34-42. The specification does not show working examples of using SEQ ID NOS: 583 or 609 individually or together in a PCA assay.

d) The nature of the invention, protein binding assays, is complex.

e) The prior art does not show SEQ ID NOS: 583 or 609. Ghosh et al., published two years after the instant effective filing year, shows reconstitution of activity from fragments of the

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same green fluorescent protein. Ghosh et al. suggest that their fragments could be used in a PCA assay on page 5659.

f) The skill of those in the art of protein binding assays is high.

g) The prior art does not show or predict success for use of SEQ ID NOS:583 and 609 in a PCA assay.

h) The claim is broad in that it is drawn to fluorescent protein fragments that are apparently from different fluorescent proteins and that must be useful in a PCA assay, without any evidence or guidance that they can be used in a PCA assay.

The skilled practitioner would first turn to the instant specification to use the claimed fluorescent protein fragments. However, the specification does not show that the fragments are from the same protein, or provide specific guidance or working examples of using SEQ IS NOS: 583 and 609 in a PCA assay. As such the skilled practitioner would next turn for such guidance from the prior art. The prior art does not show SEQ ID NOS:583 and 609. Ghosh et al. shows that fragments of the same fluorescent protein can reassociate to restore fluorescent properties. Finally said practitioner would turn to trial and error experimentation to use SEQ ID NOS: 583 and 609 without assurance of success. Such represents undue experimentation.

#### ***Terminal Disclaimer***

9. The terminal disclaimer filed on 14 March 2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of application numbers 10/856620, 10/772021, 10/353090, 10/154758, 09/603885, and U.S. Patent Nos. 6,428,951, 6,294,330, and 6,270,964 has been reviewed and is accepted. The terminal disclaimer has been recorded.

***Double Patenting***

10. The provisional rejection of claims 1-5, 10, 11, 13, 14, and 16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5, 6, 12, and 13 of copending Application No. 10/856620 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

11. The rejection of claims 1-5, 10, 11, 13, 14, and 16 under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter in view of copending Application No. 10/856620 in the Office action mailed 20 October 2004 is withdrawn in view of the Declaration under 37 CFR 1.132 by Stephen William Watson Michnick filed 14 March 2005.

12. The provisional rejection of claims 1-7 and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 of copending Application No. 10/772021 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

13. The rejection of claims 1, 2, 3, 5-7 and 10-17 under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter in view of copending Application No. 10/772021 in the Office action mailed 20 October 2004 is withdrawn in view of the Declaration under 37 CFR 1.132 by Stephen William Watson Michnick filed 14 March 2005.

14. The provisional rejection of claims 2, 6, 7, 15, and 17 under 35 U.S.C. 101 as claiming the same invention as that of claims 74-76, 81, and 83 of copending Application No. 10/353090 is withdrawn in view of the amendment filed 14 March 2005.

15. The provisional rejection of claims 1, 2, 5-7 and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 74-83 of

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copending Application No. 10/353090 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

16. The provisional rejection of claims 1, 2, 5-7 and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 59-75, and 78-80 of copending Application No. 10/154758 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

17. The provisional rejection of claims 1, 2, 5, and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 18, and 20 of copending Application No. 09/603885 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

18. The rejection of claims 1-7, and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, and 15-18 of U.S. Patent No. 6,428,951 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

19. The rejection of claims 1-7, and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 3, 10, 23, and 25-64 of U.S. Patent No. 6,294,330 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.

20. The rejection of claims 1-7, and 10-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33 and 40 of U.S. Patent No. 6,270,964 in the Office action mailed 20 October 2004 is withdrawn in view of the terminal disclaimer filed 14 March 2005.



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21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

22. Claims 1, 6, 7 and 10, 12, 13, 15-17, and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The instant claims are anticipated by copending Application No. 10/353090, which has a different inventive entity than the instant application.

23. Claims 1, 6, 7, 10, 12, 13, 15-17, and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The copending claims are generic to the instant claims and copending Application No. 10/154758 discloses green fluorescent protein reporter molecules and mutant green fluorescent protein reporter molecules on page 38.

24. Claims 1, 10, 13, 15-17, and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The claims of copending Application No. 09/603885 are generic to the instant claims with respect to the reporter molecule, and are species of the instant claims with respect to the panel of molecules screened. The copending application discloses fluorescent protein reporter molecules in claim 18.

25. Claims 1, 6, 7, and 10, 12, 13, 15-17, and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Some claims of U.S. Patent No. 6,428,951 are generic with respect to the reporter molecule and a fluorescent, phosphorescent, or luminescent protein reporter molecule is claimed in claim 13, and the patent discloses a mutant fluorescent protein in column 24. Some of the claims in the patent are claims are species of the assayed molecules of the instant claims.

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26. Claims 1, 6, 7, 10, 12, 13, 15-17, and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Some claims of U.S. Patent No. 6,294,330 are to a method that is generic with respect to the reporter molecule and the patent claims a fluorescent, phosphorescent, or luminescent protein reporter molecule in claim 10, and disclosed mutant fluorescent protein reporter molecules in column 29. Some claims of U.S. Patent No. 6,294,330 are drawn to species of assayed molecules.

27. Claims 1, 6, 7, and 10, 13, 13, 15-17 and 19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The differences between the instant claimed methods and the methods of claims 33 and 40 of U.S. Patent No. 6,270,964 are minor, and the instant compositions are used in the methods of the issued patent. The issued patent discloses mutant fluorescent proteins in column 24.

***Response to Arguments***

28. Applicant's arguments filed 14 March 2005 have been fully considered but they are not persuasive. The applicants state that the Declaration under 37 CFR 1.132 by Stephen William Watson Michnick overcomes all rejections under 35 U.S.C. § 102(f). However the rejections maintained above have not been overcome because the Declaration does not state that Stephen Michnick is the sole inventor of the subject matter commonly claimed between the instant application and the copending application or issued patent. Therefore the Declaration does not establish that the invention is not by another.

*Conclusion*

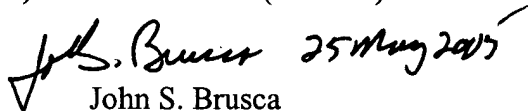
29. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 25 May 2015

John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb